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EXAMINER
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1804	8

DATE MAILED: 03/19/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 25 Nov 1991 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire THREE (3) month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449. 1 of 1
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 20 - 42 are pending in tha application.

   Of the above, daims _____ are withdrawn from consideration.

2. ☒ Claims 1-19 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 20 - 42 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or alection requiremant.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in responsa to this Office action.
9. ☐ Tha corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 thase drawings are ☐ acceptable; ☐ not acceptabla (see axplanation or Notice re Patent Drawing, PTO-948).
10. ☐ Tha proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see axplanation).
11. ☐ Tha proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the marits is closed in accordance with tha practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev.9-89)

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The specification and claims should be carefully reviewed for spelling, grammatic, and typographic error.

The rejection of claims 1-11 and 16-19 under 35 U.S.C. § 101 is withdrawn in view of cancelled claims.

The rejection of claims 2-4, 8-10, and 13-15 under 35 U.S.C. § 112, second paragraph is withdrawn in view of cancelled claims.

The rejection of claim 7 under 35 U.S.C. § 112, first and second paragraphs, is withdrawn in view of cancelled claim.

New claims 20-42 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Recited construct elements of claims 20-42 are inadequate to achieve the stated result (e.g., 3' termination sequences are missing and elements must be operably joined in claims 20, 29-32, 37 and 39-42). Furthermore, claims 37-38 appear to omit method steps e.g., "having" suggests a previous step and "whereby" fails to define the phenotype modification; indeed, no recited element appears to modify plant phenotype in so far as this vague terminology is understood. Method claims 39-40 fail to recite any steps and do not set forth actual methods. Method claims 41-42 each recite a single step which fails to achieve what the preamble asserts.

In claim 22, "untranslated end" is vague and indefinite as 3' transcription termination regions are flanking regions not ends. Claims 24-26 are vague and indefinite as it is unclear which direction is "upstream" for DNA which is a double helix and it is not clear what else "at least approximately" includes that would not be included by the phrase, at least.

Claims 29-32 fail to distinctly claim the invention as a "CaMV 35S promoter construct" cannot be comprised of itself and still be a construct (as in claims 29 and 32 for example) such a construct would have chimeric components such as enhancers, CAAT boxes, TATA boxes and ribosome binding sites for example. Also the term "second DNA" in these claims implies that there is a first DNA but the claims do not presently describe a first DNA which leads to a confusing antecedent basis for the sequences of interest in claim 30. Claim 31 lacks antecedent basis for "CaMV 35S promoter cassette" and it is not possible for promoters to be "further comprised" of transcript termination regions (claims 31-32). Claim 32 lacks antecedent basis for "said transcript termination region of said figwort 34S promoter construct".

Apparently "promoter" has been used in this disclosure in a non-standard way to refer to the entire 5' untranslated flanking sequence (composed of TATA box and enhancer) rather than to the polymerase binding site (TATA box) which promotes transcription. Consequently, "promoter" as used here already contains an untranslated leader sequence and cannot be said to "further

comprise" a leader sequence as in claims 33-34. Claims 29-32 and 41-42 are also confusing because there is no apparent interaction or relationship or structural orientation or cooperation between constructs which have CaMV promoters and constructs which have FMV promoters.

Claims 39-42 are vague and indefinite in that it is not clear what constitutes a "method of providing" and "having" appears to refer to an act not set forth in these claims. It is unclear what constitutes "expression" in claim 40. Claim 41 is vague and indefinite as it is not clear what a "similar level of transcription" would be since the "CaMV 35S promoter" is undefined (i.e. there are numerous subsets and arrangements of sequences having various activities) and the "different promoter" is unspecified; thus claim 41 is also unduly broad. The negative limitation in claim 42 also renders the claim indefinite and fails to distinctly set forth the invention. Claim 42 depends from a cancelled claim.

New claims 20-42 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20, 23-26, 32, 37, and 39-40 refer to a "figwort 34S promoter" but the disclosure describes a figwort mosaic virus 34S

promoter. The chimeric promoter of claims 39-40 lacks support in that the disclosure fails to describe a "caulimovirus promoter comprising a figwort 34S promoter". Claim 42 is vague and indefinite as to what transcription levels would be considered "CaMV 35S-like"; the specification sheds no light on the issue.

New claim 41 is rejected under 35 USC § 112, first paragraph, as the disclosure is enabling only for claims limited to the FMV 34S promoter as various activities of various CaMV 35S constructs in various tissues under various conditions render a "different promoter having" similar activity not commensurate in scope with the disclosure. See MPEP §§ 706.03(n) and 706.03(z).

The rejections of claims 1-11 and 16 under 35 USC § 102(a) as being clearly anticipated by Gowda et al or Wu et al are both withdrawn in view of the Sanger Declaration filed 25 November 1991 (Paper No. 7) and cancelled claims.

The rejection of claims 1-11 and 16-17 under 35 U.S.C. § 102(a) as being clearly anticipated by Goldberg et al is withdrawn in view of the Sanger Declaration filed 25 November 1991 (Paper No. 7) and cancelled claims. Arguments directed at disclosure of both gene I and VI promoters are moot.

The rejection of claims 1-11 and 16-19 under 35 U.S.C. § 102(b) as being clearly anticipated by Shepherd et al is withdrawn in view of cancelled claims.

New claims 39-40 are rejected under 35 U.S.C. § 102(b) as being anticipated by Shepherd et al where the sequence of

interest is an FMV gene.

The rejection of claims 1-11 under 35 U.S.C. § 102(b) as being clearly anticipated by Richins et al is withdrawn in view of cancelled claims.

New claims 20-21, 23-27, and 33-34 are rejected under 35 U.S.C. § 102(b) as being anticipated by Richins et al which disclosed cloned XbaI fragments joined in a 5' to 3' direction to ß-galactosidase.

The rejection of claims 1-19 under 35 U.S.C. § 103 as being unpatentable over Shah et al and Sanders et al taken with either Richins et al or Gowda et al or Wu et al or Goldberg et al is withdrawn in view of cancelled claims.

New claims 20-42 are rejected under 35 U.S.C. § 103 as being unpatentable over Shah et al and Sanders et al taken with Richins et al and Shepherd et al.

Each of the primary references disclosed all features of the present invention (including constructs with genes of interest controlled by two different strong, constitutive promoters one of which was a CaMV 35S promoter) but did not identify FMV 34S as an alternative viral promoter. Richins et al disclosed the FMV 34S promoter sequence and taught that it was analogous to CaMV 35S in position, structure, and function and, likewise, expected to have similar strong expression characteristics. This was echoed by Shepherd et al which taught that FMV was as amenable to cloning manipulation as CaMV. Shepherd et al described the broad host

range and high titer achievable with FMV in plant host cells and also compared CaMV and FMV promoters. At the time this invention was made, it was obvious to one of ordinary skill in the art to modify the primary references with the teachings of the secondary references in order to obtain high levels of expression of genes of interest in host plant cells with yet another strong viral promoter source. The extensive comparative analogy drawn with CaMV would have led one of ordinary skill in the art to reasonably expect to obtain high levels of constitutive expression with analogous FMV promoters. Thus the invention as claimed was very clearly prima facie obvious as a whole over the prior art in the absence of clear and convincing evidence to the contrary.

Applicant's arguments filed 25 November 1991 have been fully considered in so far as they apply to the above rejection, but they are not deemed to be persuasive. Arguments which go to deficiencies of individual primary references fail to overcome a rejection based on a combination of references. It is not clear what applicant is talking about (at page 9) with respect to modifying CaMV 35S for decreased expression or what decreasing expression could possibly have to do with the present invention as disclosed and claimed. Shah et al clearly taught alternative use of other promoters including viral promoters.

Richins et al need not demonstrate chimeric constructs because absolute predictability is not required. The "subjective

choice of sequence which best corresponded with the TATA box of CaMV" (page 8464, Richins et al) resulted in a teaching that sequences found at position 6893 in Figure 1 of this reference were comparable to CaMV 35S (see Figure 5 which aligned the two regions). This is the region claimed in this application and Richins et al further called attention to it as being "essential for high level expression of eucaryotic genes including those of plants" (page 8460, Richins et al). Thus, attention was directed away from any other TATA-like sequence. Downstream homology that went to further close similarities between FMV and CaMV was not presented as a promoter and there was no suggestion to look elsewhere for promoter activity analogous to CaMV 35S.

Assertions that comparable levels of activity are unexpected lack persuasive force. Both secondary references stressed comparability of FMV and CaMV. Since 5' flanking transcription and translation regulatory regions were known to be ensembles of components whose location extended for some distance upstream of the structural gene, flanking regions were routinely cloned as a unit of anywhere from at least 200 to a 1000 or more nucleotides. It would have been well within the ordinary level of skill in this art to clone such a 5' region with a reasonable expectation of encompassing the entire regulatory region guided by analogy to the size of the CaMV 35 region disclosed in the primary references. Consequently, a reasonable expectation of success did not depend upon a search for enhancer consensus sequences.

Furthermore, since FMV was known to successfully and severely infect host plants and to reach a high titer in plant cells, it would have been reasonable to expect the promoters to be highly expressed and in view of the emphasis of the prior art teaching to be comparable to CaMV activity.

Assertions that unexpected results are found in the absence of tissue specificity are not persuasive and constitute a misreading of Teeri et al and Ow et al. These references chop up the CaMV 35S into subset sequences having different properties when used separately or in various rearranged combinations. Intact CaMV 35S as taught by the cited primary references is not tissue specific. Applicant's references provide an explanation for why the intact CaMV 35S promoter is active in all tissues if at least some subset sequences are recognized and compatible with any given tissue. Constitutive expression differs from tissue specificity and is unrelated to applicant's argument (at page 11) but intact CaMV 35S was a well-known constitutive promoter that was expressed in all tissues like the present invention. Thus the invention as claimed was very clearly prima facie obvious as a whole over the prior art in the absence of clear and convincing evidence to the contrary.

No claim was allowed.

Any inquiry concerning this communication should be directed to P. Rhodes at telephone number (703) 308-0196.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Elizabeth C Weimar

ELIZABETH C. WEIMAR
SUPERVISORY PATENT EXAMINER
ART UNIT 184

P. Rhodes PLR
February 18, 1992